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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,512	12/12/2003	Salman Al-Mahmood	1414-03	6845

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EXAMINER	
MCGARRY, SEAN	
ART UNIT	**PAPER NUMBER**
1635	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,512	AL-MAHMOOD, SALMAN	
	Examiner	Art Unit	
	/Sean R. McGarry/	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-27* is/are pending in the application.

4a) Of the above claim(s) *7-18 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,19,20,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 6/14/2001. It is noted, however, that applicant has not filed a certified copy of the French application as required by 35 U.S.C. 119(b). It is now noted that applicant has indicated in the response filed 4/30/07 that a certified copy of the French patent Application will follow in due course. No certified copy has been received by the Office as of the date of this Official Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 6, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4, 26, and 27 all recite "capable of hybridizing under strict conditions". It is not clear what compounds would be embraced by the term "capable of hybridizing under strict conditions". This is because there is no clear definition of the terms such that the metes and bounds of the claim have been clearly set. There are many hybridization conditions in the art that may be considered "strict" or stringent and would include highly stringent or moderately stringent etc. There is no art-recognized definition of "strict conditions" and the specification as filed fails to provide a definition of what those conditions are. Hybridization conditions vary from one biological assay to another. One in the art is left without any clear demarcation of where the metes and bounds of the invention may lay. If applicant believes that the specification does provide a specific definition, applicant should point to the definition with particularity. Claim 6 is rejected as far as it depends from claim 4.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Surmacz et al. Clinical Cancer Research Vol. 1.

Surmacz et al disclose an antisense composition that was administered to MCF-7 cells. The antisense composition comprises an antisense oligonucleotide that comprises at least 12 nucleotides that bind to SEQ ID NO: 28 at the nucleotides down stream of the start codon, for example. The antisense oligonucletide comprises at least 12 contiguous nucleotides to SEQ ID NO: 28 and has been clearly demonstrated to inhibit human IRS1 in human cells.

Applicant's arguments filed 4/30/07 have been fully considered but they are not persuasive. Applicant argues that the instant claims are limited to human sequences. It is noted that claim 1 provides nothing that would point to any particular organism. Claim 3 only requires a contiguous 12 nucleotides antisense to SEQ ID NO:28.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Wolf et al [The Journal of Biological Chemistry Vol. 270 (46):27404-27410, 1995].

Wolf et al disclose the human IRS1 cDNA in vectors (see "Material and Methods" section, for example). The vectors disclosed would comprise the SEQ IDS recited in the claims since the vectors are double stranded and the recited SEQ ID NOS are from the human IRS1 sequence.

Applicant's arguments filed 4/30/07 have been fully considered but they are not persuasive. Applicant argues that Wolf does not disclose the recited sequences. The

recited sequences are human IRS1 sequences. The sequences in the vectors disclosed by Wolf are human IRS1 sequences. The vectors therefore are nucleic acid sequences that comprise the recited human IRS1 sequences.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148].

The claimed invention is drawn to a pharmaceutical composition comprising an antisense molecule that inhibits IRS1 expression including and IRS1 of SEQ ID NO: 28 where the antisense is an antisense sequence of a coding region of SEQ ID NO:28 that has at least 12 contiguous nucleotides. The invention also includes where the composition comprises a range of active ingredient capable of specified modes of delivery, and also where the composition comprises a pharmaceutically acceptable carrier.

Surmacz et al disclose an antisense composition that was administered to MCF-7 cells. The antisense composition comprises an antisense oligonucleotide that comprises at least 12 nucleotides that bind to SEQ ID NO: 28 at the nucleotides down stream of the start codon, for example. Surmacz has taught the administration of

antisense oligonucleotides at a concentration of 80micrograms/ml and at 120micrograms/ml to inhibit expression of IRS1 in breast cancer cells. Surmacz et al disclose that over expression of IRS1 may play an important role in the loss of hormone dependence of breast cancer cells and contribute to the phenotypic changes associated with malignant progression.

Nolan et al disclose the inhibition of IRS1 expression in breast cancer cells via vectors that express anti-irs-1 clones. Nolan et al indicate that IRS1 may regulate the proliferation of tumor cells, see page 828, for example. Nolan et al have shown that significant reduction of IRS1 levels in breast cancer cells results in apoptotic cell death (see pages 831-832, for example).

The above references have shown that the art has used antisense compounds in the research of a biochemical pathway involving IRS1 and breast cancer cells. The prior art has shown that inhibition of IRS-1 in breast tumor cells results in apoptotic cell death of the cancer cells. The prior art above does not specifically disclose the use of pharmaceutical carriers.

Bennett et al teaches that at the time of invention the art was replete with pharmaceutically acceptable carriers that could be used in cell culture to enhance antisense uptake and used in *in vivo* applications. Bennett et al have disclosed at column 5 that antisense compounds are commonly used as research reagents to determine the function of genes and to distinguish between functions of various members of a biological pathway. At column 5 it is also disclosed that antisense oligonucleotides have been employed for therapeutic uses. At columns 12-25 a

multitude of carriers are disclosed for the artisan to choose from. One in the art would have know at the time of filing, based on the disclosure of Bennett et al that dosages are routinely established for the particular application at hand and also that one would choose an appropriate carrier for the application at hand. One in the art interested in inhibiting IRS-1 in cells in culture or in an animal model of breast cancer would clearly have an arsenal of well know carriers from which to choose.

The combination of references above clearly show the claimed invention. One in the art would clearly have been motivated to use antisense compositions to determine IRS1 function in at least breast cancer cells in culture and further would be motivated to make such compositions to test in animal models of cancer, for example.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Applicant's arguments filed 4/30/07 have been fully considered but they are not persuasive. Applicant again argues as if the claims are limited to human (see above). It is noted that the antisense molecules used in the prior art do indeed inhibit the activity of human IRS1 in human cells. Applicant also argues over the capacity to inhibit angiogenesis. It is the position of the examiner that the prior art antisense oligonucleotides meet the structure required by the claims. There is no reason to believe that the instant claims define over the prior art where applicant has discovered some new structure required for the antisense to have this ability. It appears from

applicant disclosure that any antisense targeted to SEQ ID NO: 28 would have this capacity. In any event applicant can note the below.

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Applicant asserts that Bennett teaches away from the instant invention. Applicant has left it up to the examiner to determine why this is the case and the examiner asserts that the Bennett reference does not teach away and is relied upon for the reasons set forth in the Official action.

Claims 19 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148] as applied to claims 1, 3, 5, 6 above, and further in view of Wolf et al.

Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148] are relied upon as above and further it is noted that Surmacz et al disclose that the human and mouse sequences of IRS1 are 90% identical and that because of this conserved structure the mouse IRS-1 is fully functional in human breast cancer cells. It is also noted that the vectors used by Nolan et al contained the mouse antisense sequence. Wolf et al disclose that the human sequence was known. It clearly would be obvious to use a human IRS sequence expressed in the antisense orientation to inhibit human IRS-1 expression. It appears that it was a matter of convenience for the

artisans to use a construct already made an available for use in human breast cancer cells, but clearly the use of a human antisense sequence to inhibit a human sequence would be an obvious option. It is noted that the specified sequences of claim 19 would all be comprised in an antisense expressed from a human antisense IRS-1 vector.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Applicant's arguments filed 4/30/07 have been fully considered but they are not persuasive. Applicant again argues that the prior art does not teach the recited sequences of claim 19 and then argues limitations not in the claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Sean R. McGarry/ whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean R McGarry/
Primary Examiner
Art Unit 1635